REMARKS

Status of the Claims:

Claims 1 through 105 are pending. Claims 6 through 10, 12 through 14, 26 and 44 through 105 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1 through 5, 11, 15 through 25 and 27 through 43 stand rejected by the Examiner. Claim 1 has been amended. Claim 21 has been canceled, and the limitations thereof incorporated into amended Claim 1. Claims 1 through 5, 11, 15 through 20, 22 through 25, and 27 through 43 are pending and being examined on the merits. It is believed that no new matter has been introduced by way of the amendments herein.

Rejection under 35 U.S.C. §112, Second Paragraph:

Claim 13 has been rejected by the Examiner under 35 U.S.C. §112, second paragraph, as being "incomplete for omitting essential elements". Applicants respectfully traverse this rejection for the following reasons.

In particular, the Examiner is concerned with the absence of a recited "buffer" in claim 1, since the Examiner views the buffer as an essential element. It is Applicants' position that independent claim 1 recites a buffer and its corresponding function in a manner compliant with the requirements of 35 U.S.C. §112. Indeed the buffer is important to the claimed invention and is recited in claim 1. Applicants know of no legally sound reason at this time in the prosecution to further narrow the buffer element to a particular species, as is apparently being suggested by the Examiner.

The claims are fully compliant with the requirements of 35 U.S.C. §112, second paragraph. This rejection should, therefore, be withdrawn.

Rejection under 35 U.S.C. §102:

Claims 1-5, 15, 16, 18-25, 27-28, 30-42 have been rejected by the Examiner under 35 U.S.C. §102(b) as being anticipated by Zhang et al. U.S. Patent No. 6,264,981. Applicant respectfully traverse this rejection for the following reasons.

The Examiner argues that Zhang et al. teach a pharmaceutical dosage form comprising an ionizable pharmaceutical agents, excipients and buffers. The Examiner further argues that sorbitol is a well-known sugar substitute and asserts that it would be bioequivalent to the sugar amount in a given dosage form.

A claim is anticipated within the meaning of 35 U.S.C. §102 when a single prior art reference discloses each and every element required by the claim. For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. Scripps Clinic & Res. Found.v. Genentech, Inc., 927 F.2d 1565, 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991).

At the onset, the Examiner appears to have misread the claimed invention with respect to the bioequivalency feature. The bioequivalency accomplished by the instant invention refers to that of the active pharmaceutical ingredient – not specifically the sugar-substitute to the sugar. Put another way, the bioequivalency refers to the equivalent plasma concentration achieved with the *active* ingredient as delivered using the claimed formulation as compared to a sugar-based formulation.

Furthermore, the sorbitol example cited by the Examiner (column 12, Example 2) is contained in a formulation with droperidol as the active ingredient. Independent Claim 1 has been amended to limit the pharmaceutically active ingredient to fentanyl and its pharmaceutically acceptable salts. Furthermore, the Examiner's attention is invited to

the proper context of the use of sorbitol in Zhang at column 7, second complete paragraph, which clearly lists sorbitol as a *dissolution* agent – and not in the context of a sugar substitute. No discussion is seen within Zhang et al. that fairly teaches or suggests formulating a solid oral transmucosal fentanyl-containing pharmaceutical composition as a sugar-free composition in a manner which anticipates the claimed invention. Accordingly, as a result of the absence of teachings within Zhang et al. required by the claimed invention at hand, it cannot be said that Zhang et al. anticipates the claimed invention.

The claimed invention is not anticipated by the above reference within the proper meaning of 35 U.S.C. 102. This rejection should, therefore, be withdrawn.

Rejection under 35 U.S.C. §103:

Claims 1-5, 11, 15-25, 27-42 have been rejected by the Examiner under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. U.S. Patent No. 6,264,981 in view of Serpelloni et al. U.S. Patent No. 5,629,042 or Burgard et al. U.S. Publ. Appl. No. 2001/0029959. Applicants respectfully traverse this rejection for the following reasons.

The shortcomings of the Zhang et al. reference are discussed in the above response to the rejection under 35 U.S.C. §102(b), and are likewise applicable and repeated herein. The Examiner further argues that Zhang et al. teach a buffer in an amount sufficient to maintain a portion of the active in ionized form. The Examiner relies upon Serpelloni et al. for a teaching of isomalt as a sugar substitute in hard candies, and Burgard et al. for a teaching of isomalt as a sweetener.

Applicants have amended independent claim 1 to recite fentanyl and its pharmaceutically acceptable salts as the pharmaceutically active ingredient. Applicants

have accomplished a pharmaceutical composition for oral transmucosal administration of fentanyl (and salts thereof) which is sugar-free and bioequivalent to the sugar-containing composition. As explained on page 17 of Applicants' specification, achieving a sugar-free oral transmucosal composition, wherein the active ingredient affects the central nervous system, should also achieve bioequivalency for those patients accustomed to the sugar-based pharmacokinetics, e.g., rate and extent of absorption. This reduces the risk of overdosage to the patient.

As further explained on page 19, it is generally found that sugar-free oral transmucosal solid dosage forms are not bioequivalent to their corresponding sugar-containing version –possibly for a variety of physical and chemical factors. Accordingly, and contrary to the Examiner's position, it is not simply a matter of "swapping" sorbitol for sucrose. Applicants' bioequivalency data demonstrates that Applicants have accomplished the desired bioequivalency with a sugar-free formulation of fentanyl.

Although there are common ingredients shared between both fields, the proper context of the Serpelloni et al. technology is candy-making or the confectionary art. The proper context of one of ordinary skill for purposes of the instant invention, however, is the pharmaceutical field. A screw can be used in a wide variety of technologically unrelated fields – from car engines to tables and chairs, and the simple fact that a screw can be shared by various technologies does not automatically render them relevant contexts for purposes of obviousness. Similarly, flavorings, sweeteners, and the like can be shared by various fields but do not necessarily render the fields using them as related for obviousness purposes to one of ordinary skill. Furthermore, the hard-boiling process of Serpelloni et al. for the manufacture of candy, is not automatically an appropriate technique for all orally administrable pharmaceutical compositions.

Burgard et al. is directed to a nicotine-containing gum or tablet with sweeteners. There is nothing seen in Burgard pertaining to fentanyl or oral transmucosal absorption. At best, the reference teaches the use of isomalt as a sugar alcohol that can be used to prepare nicotine gum or tablet (see Example 5). It is not seen how the disclosure of Burgard et al. brings Zhang et al. closer to the claimed invention.

The Examiner's arguments appear to be premised on the erroneous view that ingredients can be readily interchanged, "swapped" or simply added to various dosage forms with expected success. On the contrary, formulating dosage forms requires accommodation of the chemical relationships, or "interplay" between the various ingredients to accomplish a net successful resultant dosage form. Oftentimes, chemical compatibility between ingredients can be unpredictable. There's no teaching or suggestion in either Serpelloni or Burgard as to how to formulate excipients in a "sweet" for transmucosal absorption of a pharmaceutically active ingredient.

It is not seen why one of ordinary skill in the pharmaceutical field would have combined candy-related teachings of isomalt and sorbitol (of Serpelloni and Burgard) into a particular pharmaceutical composition using sorbitol with droperidol (of Zhang). It is further not understood why one of ordinary skill in the art would have been lead or motivated to arrive at the claimed invention thusly, the invention which is directed to oral transmucosally absorbed fentanyl sugar-free solid that is bioequivalent to a sugar-containing composition by virtue of the buffer. The references applied by the Examiner fail to provide a combination of teachings that fairly teach or suggest the claimed invention to one of ordinary skill in the art. Therefore, the Examiner has not established a *prima facie* case of obviousness to support a rejection on obviousness grounds.

Given the above, the claimed invention is not unpatentable in view of the above references within the proper meaning of 35 U.S.C. §103. This rejection should, therefore, be withdrawn.

Conclusion:

In view of the above amendment and/or remarks, it is believed that the application is now in condition for allowance. Accordingly, prompt communication to that effect is earnestly solicited. The Examiner is invited to contact the undersigned to discuss the application if it is deemed appropriate to expedite examination on the merits.

Respectfully submitted,

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